



hereditary sensory and autonomic neuropathy type IE

Hereditary sensory and autonomic neuropathy type IE (HSAN IE) is a disorder that affects the nervous system. Affected individuals have a gradual loss of intellectual function (dementia), typically beginning in their thirties. In some people with this disorder, changes in personality become apparent before problems with thinking skills.

People with HSAN IE also develop hearing loss that is caused by abnormalities in the inner ear (sensorineural hearing loss). The hearing loss gets worse over time and usually progresses to moderate or severe deafness between the ages of 20 and 35.

HSAN IE is characterized by impaired function of nerve cells called sensory neurons, which transmit information about sensations such as pain, temperature, and touch. Sensations in the feet and legs are particularly affected in people with HSAN IE. Gradual loss of sensation in the feet (peripheral neuropathy), which usually begins in adolescence or early adulthood, can lead to difficulty walking. Affected individuals may not be aware of injuries to their feet, which can lead to open sores and infections. If these complications are severe, amputation of the affected areas may be required.

HSAN IE is also characterized by a loss of the ability to sweat (sudomotor function), especially on the hands and feet. Sweating is a function of the autonomic nervous system, which also controls involuntary body functions such as heart rate, digestion, and breathing. These other autonomic functions are unaffected in people with HSAN IE.

The severity of the signs and symptoms of HSAN IE and their age of onset are variable, even within the same family.

Frequency

HSAN IE is a rare disorder; its prevalence is unknown. Small numbers of affected families have been identified in populations around the world.

Genetic Changes

HSAN IE is caused by mutations in the *DNMT1* gene. This gene provides instructions for making an enzyme called DNA methyltransferase 1. This enzyme is involved in DNA methylation, which is the addition of methyl groups, consisting of one carbon atom and three hydrogen atoms, to DNA molecules.

DNA methylation is important in many cellular functions. These include determining whether the instructions in a particular segment of DNA are carried out or suppressed (gene silencing), regulating reactions involving proteins and fats (lipids), and controlling the processing of chemicals that relay signals in the nervous system (neurotransmitters). DNA methyltransferase 1 is active in the adult nervous system.

Although its specific function is not well understood, the enzyme may help regulate nerve cell (neuron) maturation and specialization (differentiation), the ability of neurons to migrate where needed and connect with each other, and neuron survival.

DNMT1 gene mutations that cause HSAN IE reduce or eliminate the enzyme's methylation function, resulting in abnormalities in the maintenance of the neurons that make up the nervous system. However, it is not known how the mutations cause the specific signs and symptoms of HSAN IE.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In most cases, an affected person has one parent with the condition.

Other Names for This Condition

- DNMT1-related dementia, deafness, and sensory neuropathy
- hereditary sensory and autonomic neuropathy type 1 with dementia and hearing loss
- hereditary sensory neuropathy type IE
- HSN IE
- HSNIE

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Hereditary sensory neuropathy type IE
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C3279885/>

Other Diagnosis and Management Resources

- GeneReview: DNMT1-Related Dementia, Deafness, and Sensory Neuropathy
<https://www.ncbi.nlm.nih.gov/books/NBK84112>
- University of Chicago: Center for Peripheral Neuropathy
<http://peripheralneuropathycenter.uchicago.edu/>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>

- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Encyclopedia: Dementia
<https://medlineplus.gov/ency/article/000739.htm>
- Encyclopedia: Sensorineural Deafness
<https://medlineplus.gov/ency/article/003291.htm>
- Health Topic: Degenerative Nerve Diseases
<https://medlineplus.gov/degenerativenervediseases.html>
- Health Topic: Dementia
<https://medlineplus.gov/dementia.html>
- Health Topic: Hearing Disorders and Deafness
<https://medlineplus.gov/hearingdisordersanddeafness.html>
- Health Topic: Peripheral Nerve Disorders
<https://medlineplus.gov/peripheralnervedisorders.html>

Genetic and Rare Diseases Information Center

- Hereditary sensory and autonomic neuropathy type 1E
<https://rarediseases.info.nih.gov/diseases/11927/hereditary-sensory-and-autonomic-neuropathy-type-1e>

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Dementia Information Page
<https://www.ninds.nih.gov/Disorders/All-Disorders/Dementia-Information-Page>

Educational Resources

- MalaCards: dnmt1-related dementia, deafness, and sensory neuropathy
http://www.malacards.org/card/dnmt1_related_dementia_deafness_and_sensory_neuropathy
- Orphanet: Hereditary sensory and autonomic neuropathy type 1
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=36386
- Washington University in St. Louis Neuromuscular Disease Center
<http://neuromuscular.wustl.edu/time/hsn.htm#dnmt1>

Patient Support and Advocacy Resources

- Family Caregiver Alliance
<https://www.caregiver.org/>
- Hearing Health Foundation
<http://hearinghealthfoundation.org/>
- The Foundation for Peripheral Neuropathy
<https://www.foundationforpn.org/>

GeneReviews

- DNMT1-Related Dementia, Deafness, and Sensory Neuropathy
<https://www.ncbi.nlm.nih.gov/books/NBK84112>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22hereditary+sensory+and+autonomic+neuropathy+type+IE%22+OR+%22Hereditary+Sensory+and+Autonomic+Neuropathies%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28hereditary+sensory+neuropathy%29+AND+%28deafness%29+AND+%28dementia%29%29+OR+%28%28dnmt1%29+AND+%28neuropathy%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D>

OMIM

- NEUROPATHY, HEREDITARY SENSORY, TYPE IE
<http://omim.org/entry/614116>

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